Individualizing prostate cancer treatment

Impact Paragraph

Social relevance and target groups

Prostate cancer is a very common cancer type, and although mortality rates are low, it touches the lives of a large number of men. This disease has a range of viable treatment options and a large number of clinical parameters and biomarkers predictive for the primary outcome of these treatments, as well as treatment related side effects. Ideally these factors should therefore guide optimized treatment selection. In practice, however, this is rarely applied and treatment selection is often based on factors largely unrelated to the patients clinical characteristics and treatment outcomes.

Both previously published studies and the research done in this thesis suggest that the quality of life of prostate cancer patients has the potential to be improved through personalized treatment selection. This, combined with the large number of patients diagnosed every year, effectuates optimized treatment selection would have large social impact.

The primary aim of this thesis was to combine existing models predictive of treatment outcome and published biomarkers into clinical decision support systems in order to bridge the gap between literature and clinical practice. This has as an advantage that the large number of clinical factors such as disease parameters, treatment parameters, patient characteristics and genetic markers could be condensed into an easy to handle number of factors, such as expected cure rate, risk of treatment related side-effects and cost-effectiveness. Since the human cognitive ability is limited, and only a number attributes can be recalled during decision making, this condensation of information would streamline the decision making process. Therefore not only the patient is ultimately benefited by the application of such tools, but clinical professionals will be empowered during treatment selection as well.

Primary findings and products

The primary output of the work presented in this thesis are the methodologies and algorithms that form the basis of the developed decision support systems. All the studies published in this thesis suggest that the application of these models in a clinical environment has the potential to improve the quality of life of patients, often providing monetary value, which underscores the advantage of the developed decision support systems.

The methodologies have been published and described in great detail, sufficient for anyone with access to the publications to replicate the work that was done. This makes it possible for the methods used to be applied in other projects, either for different ends or to follow-up the work that was published.

In addition to the descriptions of model parameters and methods, the code written to implement the decision support systems and generate the results presented in

this thesis were made available on GitHub, so that they may be applied, reused, adapted and improved in future projects. The models as a whole will also be made available on a public platform currently under construction.

Innovation

The platform that forms the basis of all the decision support systems presented in this thesis incorporate different models and combine them in a single application. Models eligible for integration are those that predict outcome or toxicity, dose metrics or cost-utility. From a scientific point of view this is beneficial as the methods described combine separate instances of previously published models and biomarkers and provides a bridge for them to be directly applied towards the benefit of the clinical professional and the patient. This improves the prospects with respect to the usefulness and impact of valuable scientific research. To our knowledge, our methods are the first within the field of prostate cancer that work to actively selecting, refining and adapting existing knowledge towards clinical benefit in such a manner.

As mentioned before, the methodologies and code have been made available for further use. Especially the Markov model described in Chapter 7 was developed and described in great detail, including transition probabilities to a large number of health states and detailed descriptions of treatment costs. This information can prove invaluable for other researchers looking to build a cost-effectiveness model concerning the primary treatment of prostate cancer, as many of these model parameters can be recycled, which would streamline and simplify this part of the work for future researchers.

The method for generating synthetic patients is an emerging field, and has to potential to be useful to validate newly developed models against published clinical trials, even when available patient and treatment parameters are incomplete, such as was done in Chapter 7. This allows for relatively cheap and fast testing of models prior to (and potentially to inform) setting up expensive and time consuming retrospective or prospective clinical trials. Similarly, the in silico trial is a possible application of the synthetic patient datasets. An in silico trial could be used to test new methods or technologies, as well as to gain insight into underrepresented patient populations. The information gained from this could be used to better prepare prospective or retrospective clinical trials prior to investing the time and expenses required of such a project. This could result in better designed clinical trials and possibly preventing waste in the form of effort, time and money.

Implementation

As discussed in the general discussion of this thesis, the developed decision support systems require improvement, optimization, expansion and (prospective)

validation before further steps can be made toward introducing them into clinical practice. Projects have already been set up for these developments, one of which with the particular aim of including active surveillance into the framework and validation on a patient cohort through a clinical trial. In parallel, work is being done to adapt the framework presented here into a personalized patient decision aid.

When these important developments have taken place, the framework could be properly developed into a software application that would be suitable for commercial use. This development should take place with close cooperation between the developing party (such as a company or a research group) and the potential end users (clinical professionals). This final product could then be subjected to regulatory bodies and presented to hospitals and clinics. This would make the technologies developed in this work available to the end user (the medical professional) and the target group (prostate cancer patients) and potentially improve the quality of life for this patient population.